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Award Number: W81XWH-12-1-0143

TITLE: Social Resources That Preserve Functional Independence After Memory Loss

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REPORT DATE: May 2015

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE		*Form Approved OMB No. 0704-0188*
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1. REPORT DATE May 2015	**2. REPORT TYPE** Annual	**3. DATES COVERED** 20 April 2014 – 19 April 2015
4. TITLE AND SUBTITLE: Social Resources That Preserve Functional Independence After Memory Loss		**5a. CONTRACT NUMBER**
		5b. GRANT NUMBER W81XWH-12-1-0143
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) Dr. M. Maria Glymour, Dr. Thu Nguyen, Dr. Pamela M. Rist		**5d. PROJECT NUMBER**
		5e. TASK NUMBER
E-Mail: mglymour@psg.ucsf.edu		**5f. WORK UNIT NUMBER**
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of California San Francisco Dept of Epidemiology and Biostatistics 550 16th Street, 2nd Floor San Francisco, CA 94143		**8. PERFORMING ORGANIZATION REPORT**
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		**10. SPONSOR/MONITOR'S ACRONYM(S)**
		11. SPONSOR/MONITOR'S NUMBER(S)
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited		
13. SUPPLEMENTARY NOTES		

14. ABSTRACT *(Enter a brief (approximately 200 words) unclassified summary of the most significant finding during the research period.)*

We used a large, diverse, longitudinal study of middle aged and older Americans to identify social factors that help individuals preserve functional independence in basic and instrumental ADLs as long as possible, even in the context of declining memory or severe memory impairment. We found strong associations between decreased cognitive functioning and incident ADL and IADL limitations. Physical activity may help to decrease the risk of ADL and IADL limitations even among those with cognitive impairment, while smoking and depression may increase the risk of incident ADL limitations among those with cognitive impairments. We also found that physical activity is associated with lower risk of future nursing home admission, another powerful indicator of functional independence. Although most family level variables were not associated with independence outcomes, being married and spouse's education and (less) depression predicted better functional outcomes. Finally, our results indicate that several features of neighborhood, including perceived safety, disorder, and cohesion predict IADL outcomes, in individuals with or without memory impairments. By managing conventional risk factors, it may be possible to stave off dependencies, maximize quality of life, and minimize caregiver burden.

15. SUBJECT TERMS Disability, functional independence, activities of daily living, instrumental activities of daily living, individual, family, community, dementia, memory impairment

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION**	**18. NUMBER**	**19a. NAME OF RESPONSIBLE PERSON** **USAMRMC**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER**
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1. INTRODUCTION

Memory losses are common among long-term survivors of traumatic brain injury (TBI) and TBI has been linked to increased risk of memory impairment and dementia. This is an important determinant of long-term well-being for military service men and women and their families, because of the elevated incidence of TBI in combat areas. Memory and cognitive impairments predict substantial losses in ability to independently manage daily activities; this loss of independence can be devastating to the individual and his or her family. To avoid dependence, we need to identify factors which preserve independence even in the face of memory and cognitive losses. While studies have examined predictors of institutionalization among those with dementia(*1*), factors like depression which predict institutionalization may be undertreated among those with dementia.(*2*) It is not known whether managing these risk factors among individuals with cognitive impairment is important because little research has been done on whether resources at personal and environmental levels can modify the translation of impairments caused by neurodegenerative diseases into functional disabilities. Current understanding of disability emphasizes that physical impairments in body functioning or structure do not necessarily induce functional disability because environmental, behavioral, and instrumental accommodations can foster continued independence.(*3*) Individual level modifiers for example, physical activity or not being depressed, and family level modifiers for example, spouse's education and contacts with friends and family, may also influence functional limitations and the individual's ability to use accommodations or coping strategies and may help promote functional independence even among individuals with memory loss or dementia. We proposed to use data from the nationally representative Health and Retirement Study (HRS), a large, diverse, longitudinal study of middle aged and older Americans, to identify modifiable individual-, family-, and community level factors that help individuals preserve functional independence as long as possible even in the context of declining memory or cognitive impairment.

2. KEYWORDS

Disability, functional independence, activities of daily living, instrumental activities of daily living, individual, family, community dementia, memory impairment

3. ACCOMPLISHMENTS

1. Estimate the association between memory/cognitive losses and changes in functional independence in HRS cohort members (Q3 2012)
2. Test individual level resiliency factors as modifiers of the effects of memory on functional impairments in longitudinal models (Q3 2012 through Q1 2013)
3. Link family level variables and test family level resiliency factors as modifiers of the effects of memory functional impairments (Q1 2013 through Q3 2013)
4. Test community level resiliency factors as modifiers of the effects of memory on functional impairments (Q1 2015 through Q1 2016; 70% completed)
5. Characterize neighborhood resources using ecometric methods, linking other data, e.g. Census and American Community Survey to (Q1 2015 to Q4 2015).
6. Summary models identifying most powerful modifiable factors promoting independence despite memory loss (Q1 2016 through Q3 2016)

What was accomplished under these goals?

- Developed inverse probability weighting models to statistically account for selective survival and dropout.
- Completed statistical programming, specified core statistical models and derived preliminary estimates of the association between cognitive loss as measured by a dementia probability score and changes in functional independence as measured by five Activities of Daily Living (ADL) and five Instrumental Activities of Daily Living (IADL) in Health and Retirement Survey (HRS) cohort members.
- Tested individual level resiliency factors as modifiers of the effects of cognitive impairment on ADL limitations using pooled logistic regression and Poisson regression as well as inverse probability weighting.
- Published a manuscript on cognitive impairment, individual-level modifiers and incident ADL limitations.
- Published a manuscript on cognitive impairment, individual-level modifiers and incident IADL limitations.
- Submitted abstracts to the American Academy of Neurology Annual Meeting in 2014 and the Society of Epidemiological Research Annual Meeting in 2014.
- Linked family level variables and tested family level resiliency factors as modifiers of the effects of memory functional impairments.
- Drafted manuscript presenting results from analysis of cognitive impairment, family-level modifiers, and incident I/ADL limitations.
- Began analyses examining whether neighborhood level factors were associated with incident I/ADL limitations and if these associations varied by cognitive status.
- Estimated effects of risk factors evaluated in previous papers on risk of nursing home admission as a measure of functional independence.

To accomplish the tasks outlined above, we first completed an analysis examining the impact of individual level modifiers on the association between cognitive impairment and incident ADL limitations. The complete manuscript of this analysis ("Dementia and dependence: Do modifiable risk factors delay disability?") was published in *Neurology* in 2014 and is available as an appendix. In brief, we used data from individuals enrolled in the Health and Retirement

Study. The sample included 4,922 Health and Retirement Study participants aged 65+ without limitations in activities of daily living (ADLs) at baseline. Participants were interviewed biennially up to 12 years. Cognitive status was assessed through a dementia probability score and a memory score, both of which were estimated from composites of direct and proxy assessments. We divided the dementia probability score and memory score into four categories representing low, mild, moderate or high probability of developing dementia or of having memory impairments. Our outcome was reported difficulty in any of the five activities of daily living (getting across a room, dressing, bathing, eating, and getting in and out of bed) in the past 30 days. We assessed whether physical activity, smoking, alcohol consumption, depression and income reduced the chances of incident ADL limitations for individuals across the categories of dementia risk and memory impairments, using pooled logistic regression models with inverse probability weights to adjust for time-varying confounding. We assessed multiplicative and additive interactions of dementia category with each modifier in predicting incident ADL limitations.

As expected, higher dementia score category was associated with an increased risk of ADL limitations (OR=1.65, 95% CI: 1.49-1.83 per category increase). On a relative scale, physical inactivity was associated with an increased risk of incident ADL limitations among those with low dementia probability (OR-1.51, 95% CI: 1.25, 1.81). Importantly, the interaction between physical activity and dementia probability was close to 1 and not significant, indicating that the estimated relative harm of low physical activity was similar regardless of dementia category.

In our next set of analyses, we calculated the marginal probability of developing any incident ADL limitations for each combination of modifier status and low or high dementia risk. These analyses addressed the impact of the modifiers on an absolute scale. We observed that smoking, not drinking and low income have larger adverse effects on the absolute probability of developing incident ADL limitations among those with high dementia probability than among those with low dementia probability. This suggested that even among individuals with substantial cognitive impairment managing conventional risk factors is very important and may provide a way to stave off dependencies, maximize quality of life and minimize caregiver burden. The next step in this research (not covered in the current proposal) would be to assess whether changes in these risk factors predict changes in ADL limitations and evaluate *who* among the population these risk factors influence the most, in order to better guide intervention development.

In addition to containing data on ADL limitations, the HRS cohort also assessed limitations in Instrumental Activities of Daily Living (IADLs). The manuscript titled “Do physical activity, smoking, drinking or depression modify transitions from cognitive impairment to functional disability?” was recently published in Journal of Alzheimer’s Disease. The analysis sample included 5,219 HRS participants aged 65+ without activity limitations in 1998 or 2000. Similar to the ADL analysis, we examined the impact of both memory score and dementia probability status on our outcome. We categorized memory and dementia status based on quartiles of their distributions at baseline. These categories were modeled as indicator variables due to the non-linear associations between memory impairment and incident IADL limitations. Since we were interested in examined the effect of our modifiers among those who are cognitively impaired, worst memory function or high dementia probability were used as the reference group for all analyses. Results for memory and dementia were similar so we will only discuss the results for dementia probability below.

We used the same modifiers as those used in our ADL analyses (physical activity, smoking, alcohol consumption, depression and income). Our exposure and modifier status was assessed in the wave prior to our outcome assessment. For our outcome, we used limitations in the past 30 days in IADLs. The IADLs assessed in HRS were using a telephone, taking

medication, handling money, shopping and preparing meals. Possible response options were yes, no, or do not do, which was treated as missing in this analysis. Dementia probability, categorized in quartiles, was used to predict incident IADL limitations with Poisson regression. We estimated relative (risk ratio) and absolute (number of limitations) effects from models including dementia, individual-level modifiers (physical inactivity, smoking, no alcohol consumption, and depression) and interaction terms between dementia and individual-level modifiers.

Dementia probability quartile predicted incident IADL limitations (relative risk for highest versus lowest quartile = 0.44; 95% CI: 0.28–0.70). Physical inactivity (RR = 1.60; 95% CI: 1.16, 2.19) increased the risk of IADL limitations among the cognitively impaired. The interaction between physical inactivity and low dementia probability was statistically significant (p = 0.009) indicating that physical inactivity had significantly larger effects on incident IADLs among cognitively normal than among those with high dementia probability.

In conclusion, our results suggest that maintaining physical activity should be a high priority for individuals with cognitive impairment as well as their families and clinicians because it may help to stave off dependency.

Our previous analyses have focused on the role of individual-level factors on ameliorating the impact of cognitive impairment on functional limitations. However, extensive evidence suggests that social networks also influence various domains of health, with some evidence of special importance of spouses and friends for older adults. Little is known about whether these associations prevail for onset of instrument and basic activities of daily living (I/ADLs) and whether they differ for individuals with memory impairment. The objective of the next part of our project was to determine whether family-level factors reduce the risk of incident I/ADLs and whether these associations differ for individual with high versus low dementia probability. We present an overview of our methods and results below. Our analytic sample included 4, 100 Health and Retirement Study Participants Study aged ≥65 without baseline limitations in activities of daily living (ADLs) or instrumental activities of daily living (IADLs) were interviewed biennially for up to 12 years.

The family-level variables we examined in this study included living arrangements, proximity to children, contacts with friends, spouse's depression status, spouse's employment status, and spouse's education status. We estimated the risk of incident ADL or IADL limitations using pooled logistic regression controlling for individual characteristics and cognitive function. We also explored whether dementia probability status may modify the association between family-level variables and incident I/ADL limitations.

To account for selection and attrition during the course of the study, we used inverse probability weights. Those with high dementia probability at baseline were less likely be married compared to those with lower dementia probability (Table 1). 1,500 people reported any ADL limitation and 1,496 people reported any IADL limitation during the course of the study. Table 2 shows the associations between our family-level variables and the risk of incident ADL or IADL limitations. Few family-level variables predicted incident limitations. Not being married compared to being married (ADL OR=1.14; 95% CI: 1.01, 1.30), having a depressed compared to a non-depressed spouse (ADL OR=1.56, 95% CI: 1.21, 2.00) or a spouse with less than high school education (ADL OR=1.29, 95% CI: 1.06, 1.57) compared to at least high school education predicted increased risk of incident ADL but not IADL limitations. Living with someone other than a spouse compared to living with a spouse increased risk of ADL (OR-1.35; 95% CI: 1.11, 1.65) and IADL (OR=1.30; 95% CI: 1.06, 1.61) limitations. Effects did not vary by dementia probability (Table 3). We drafted a manuscript presenting these results and will submit the manuscript to a gerontology journal this summer.

We have begun analyses to determine whether low neighborhood disorder, high neighborhood safety, social cohesion, and social ties reduced the incidence of I/ADL limitations and whether these relationships were modified by memory function. The neighborhood can represent an older adult's primary environmental context. As health declines (*4*) or the elder becomes unable to drive (*5*), more time is spent in the local community. Neighborhood social ties, perception of neighborhood safety, and neighborhood physical disorder can facilitate or restrict movement and independence.

Beginning in 2006, questions assessing neighborhood physical disorder and social cohesion were posited in each biennial HRS wave to a rotating, random sample of 50% of the core participants who completed the enhanced face to face interview. This study utilizes 2006 and 2008 data. Neighborhood variables assessing safety and social ties were asked of all the core participants in every biennial wave, but to have consistency with the timing of the neighborhood measures above, for participants answering questions regarding physical disorder and social cohesion in 2006, we used data on safety and social ties from 2006. Likewise, for participants with data on physical disorder and social cohesion in 2008, we used data for the other neighborhood variables from 2008. We fitted pooled logistic models and controlled for individual characteristics, demographics, health behaviors, and comorbidities.

In this study, we investigated four community-level factors: physical neighborhood disorder, social cohesion, neighborhood safety, and neighborhood social interaction. Participants were asked to assess the neighborhood physical order by the presence of vandalism/graffiti, vacant or deserted houses, cleanliness of the area, and whether respondents would be afraid walking home at night. The social cohesion scale measured feelings of trust, feeling part of the area, whether the respondent thinks people are friendly or would help them if they were in trouble. HRS respondents were asked how they would rate the safety of their neighborhood with response items being excellent, very good, good, fair, or poor. Lastly, we assessed social ties to neighbors. Participants were asked if they had friends in the neighborhood and separately if they had relatives in the neighborhood. They were also asked how often they get together with neighbors for a social visit. All models were adjusted for individual characteristics, demographics, health behaviors, and comorbidities.

High social cohesion, low neighborhood physical disorder, and high perceived neighborhood safety were associated with reduced incidence of IADLs limitations. Each unit increase in social cohesion was associated with an adjusted odds of developing an IADL limitation of 0.91 (95% CI: 0.86, 0.95). Each unit increase in neighborhood physical disorder is associated with an adjusted OR of 1.10 (95% CI: 1.04, 1.16). Those who reported their neighborhood level safety as being excellent, very good, or good had 32% lower odds of developing an IADL limitation compared to those who reported fair or poor neighborhood safety (95% CI: 0.52, 0.88). Neighborhood social ties did not predict IADL limitations. Although point estimates for onset of basic activities of daily living (ADLs) were consistent, none of the associations were statistically significant (Table 5).

Consistent with the previous literature, memory function was significantly related to developing limitations in instrumental activities of daily living (IADLs). Participants with a memory function score of 1.3 (~70^{th} percentile) or higher had approximately 0.7-8 times the odds of developing an IADL limitation compared to those with lower memory scores. The interactions between memory function and community level factors were non-significant (Table 6), indicating the effect of community level factors on I/ADL limitations did not vary by memory function. We also investigated whether the influence of neighborhood level factors varied by race by including an interaction between the neighborhood level factors and black race. None of the interactions terms were statistically significant.

Sensitivity analyses were done modeling memory as continuous and quadratic variables. The quadratic term for memory had high p-values ($\geq$0.7), indicating the addition of this term was not necessary. Continuous, linear memory score was significantly related with decreased odds

of developing ADLs and IADLs in all models. Effect estimates for the community level factors remained unchanged to the first decimal for both IADLs and ADLs (results not shown). Manuscript preparation for these analyses have begun, and we hope to submit in August. Additional work based on more detailed characterization of census tracts of residence using external data is planned for the summer, when final data approvals are in process.

The next priority areas for this research area are to understand whether effects are similar for veterans or other populations. The final task for this year's annual report was to "Link each study participants to census tract (CT) of residence at each interview wave." Due to delays in hiring a post-doctoral researcher and research assistant at the University of California San Francisco for this project, we have not yet begun work on this task. Since the grant has now been transferred to UCSF, we are in the process of meeting the data storage requirements to work with this restricted data in the HRS and obtaining Institutional Review Board approval for these analyses.

The original scope of the grant, which intended to identify social resources that preserve functional independence after memory loss, focused on conventional I/ADL measures as measures of 'functional independence." We realized that in our data nursing home admission is another extremely valuable measure of functional independence, so we have recently begun to apply the methods developed for this grant to examine nursing home admission as an outcome event. These analyses should be especially informative for risk factors that were found to affect either instrumental or basic ADL limitations, but not both: in some ways nursing home admission provides an even more powerful indicator of dependence. Cognitive impairment strongly predicts risk of nursing home admission(*6, 7*), more than doubling the risk of nursing home admission according to a large meta-analysis.(*6*) Given the strong association between cognitive function and risk of nursing home admission, there is a growing interest in finding factors which may delay nursing home placement even among those with cognitive impairment. Using methods which we developed as part of this grant, we have performed analyses examining effect of cognitive status and modifiable risk factors on the risk of nursing home admission. We also evaluated interactions between cognitive status and each risk factor to determine if the relative or absolute impact of each modifiable factor differs based on the individual's cognitive status. We hypothesized that physical inactivity, not consuming alcohol, and ever smoking would predict nursing home admission among individuals with normal cognitive function, but effects of these risk factors would be attenuated in both relative and absolute terms among individuals with impaired cognition.

The risk factors considered in our first analyses were physical inactivity, not consuming alcohol, and ever smoking. In addition to including dichotomized dementia probability, physical activity, alcohol consumption, and smoking status, all analyses were adjusted for demographics, socioeconomic status, and comorbidities. Our sample for these analyses included 7,631 HRS participants in the 2000 interviews who were age 65 or older and did not report a nursing home stay or living in a nursing home in 1998 or 2000. During follow-up, 2,353 people reported admission to a nursing home.

Table 7 shows the association between our risk factors and low dementia probability and risk of nursing home admission. Those with low dementia probability had a decreased risk of nursing home admission (RR=0.29; 95% CI: 0.24, 0.36) compared to those with high dementia probability. Physical inactivity compared to being active (RR=1.52; 95% CI: 1.35, 1.71), and not consuming alcohol compared to consuming alcohol (RR=1.36; 95% CI: 1.17, 1.57) predicted increased risk of nursing home admission. We observed no association between ever smoking and risk of nursing home admission (RR=0.99; 95% CI: 0.88, 1.11)

We next examined whether these factors had different effects among individuals at risk of dementia than among cognitively normal elders. There was no statistically significant interaction between dementia probability and physical inactivity (p=0.71), smoking (p=0.85), or

alcohol use (p=0.74), indicating that the relative harm of the modifier was similar for those with low and high dementia probability (Table 8).

Because similar relative effects may conceal differences in absolute effects, we also estimated the marginal probability of nursing home admission for each risk factor among those with high and low dementia probability status (Figure 1). Physical inactivity was associated with an increased absolute probability of nursing home admission for those with low dementia probability. However, the magnitude of the effect of physical inactivity on the probability of nursing home admission was slightly higher among those with high dementia probability (4.64 percentage point difference) than among those with low dementia probability (2.31 percentage point difference). Moderate drinking (compared to not consuming alcohol) predicted lower risk of nursing home admission among those with low dementia probability. Although the estimated magnitude of effect of moderate drinking on the probability of nursing home admission was higher among those with high dementia probability (4.85 percentage point difference) than among those with low dementia probability (1.52 percentage point difference), the effect was not significant among those with high dementia probability. Smoking was not significantly associated with probability of nursing home admission among those with high or low dementia probability. This project will be submitted to a journal most likely in the next two months.

Tasks to be in progress by 19 April 2015 as outlined in the statement of work:

1. Characterize neighborhood resources using ecometric methods, linking other data, e.g. Census and American Community Survey to (Q1 2015 to Q4 2015).

As mentioned above, delays in hiring a post-doctoral researcher and research assistant at the University of California San Francisco postponed progress on this task. Since the grant has now been transferred to UCSF, we are now initiating this work.

CONCLUSION

We found strong associations between decreased cognitive functioning and incident ADL limitations. Smoking, not drinking, and having low income may increase the risk of incident ADL limitations among those with cognitive impairments. Physical inactivity was associated with an increased risk of incidence IADL limitations, even among the cognitively impaired. We recently expanded the operationalization of independence in this research project to examine the influence of these individual level factors on nursing home admission risk. We observed that physical activity and moderate alcohol consumption lowered the risk of nursing home admission and the relative effects of these factors were similar for those with low and high dementia probability. In addition to our work examining the impact of individual-level factors on incident I/ADL limitations, we have also explored whether family-level modifiers influence the onset of I/ADL limitations. We observed that older adults who are not married, live with someone other than their spouse, or whose spouses have elevated depressive symptoms or low education are at higher risk of ADL limitation onset. Our investigation of neighborhood-level modifiers indicated that social cohesion, low physical disorder, and neighborhood safety reduced the risk of incident IADL limitations. These associations did not vary by cognitive function. These findings have critical importance for clinicians, patients, and family members of individuals with cognitive impairments or incipient dementia. By managing conventional risk factors and residing in a cohesive, safe, and well-maintained neighborhood, it may be possible to stave off dependencies and reduce nursing home admission risk. Additionally, spousal resources may be important opportunities to prevent disability.

Disseminating these results is particularly important because conventional risk factors for ADL limitations like depression are often undertreated among those with cognitive

impairment.(*2*) Even traditional vascular risk factors like high blood pressure, dyslipidemia, diabetes mellitus, smoking and atherosclerotic disease may be untreated in those with cognitive impairment. Maintaining healthy risk factor profiles may help individuals with incipient dementia to maintain functional independence, and thereby lower their risk for institutionalization and decrease care-giver burden. The next stages of research are needed to guide intervention and translational work, including evidence that associations we observe are causal (and therefore late life changes may still be beneficial) and identify individuals most likely to benefit from these interventions. The findings have the potential to substantially improve the quality of life of adults with memory impairments, reduce caregiving demands for family members, and delay institutionalization. This is especially important for older veterans and those with prior exposure to mild, moderate, or severe TBI, who are at elevated risk of memory loss and dementia. As the number of warfighters surviving TBI or other causes of cognitive impairment grows, it is crucial to identify the resources and tools that provide the greatest benefit to those individuals. Findings from this research can help provide guidance to individuals and families as well as clinicians, military planners, and policy makers.

What opportunities for training and professional development has the project provided?

Nothing to Report

How were the results disseminated to communities of interest?

Our primary dissemination method to date has been via the scientific literature, because at this early stage of research, other researchers considering intervention design are the primary audience.

What do you plan to do during the next reporting period to accomplish the goals?

We plan to submit our results for cognitive impairment, family-level factors, and incident I/ADLs limitations in Gerontology this summer.

We plan to submit our results for cognitive impairment, neighborhood level factors, and incident I/ADL limitations to a peer-reviewed journal in August.

We plan to complete our remaining tasks, which include:

- Characterizing neighborhood resources using ecometric methods, linking other data, e.g. Census and American Community Survey to (Q1 2015 to Q4 2015).
- Creating summary models identifying most powerful modifiable factors promoting independence despite memory loss (Q1 2016 through Q3 2016)

REFERENCES

1. M. Luppa, T. Luck, E. Brahler, H. H. Konig, S. G. Riedel-Heller, Prediction of institutionalisation in dementia. A systematic review. *Dementia and geriatric cognitive disorders* **26**, 65 (2008).
2. P. Dorenlot, M. Harboun, V. Bige, J. C. Henrard, J. Ankri, Major depression as a risk factor for early institutionalization of dementia patients living in the community. *International journal of geriatric psychiatry* **20**, 471 (May, 2005).
3. A. M. Jette, Toward a common language for function, disability, and health. *Physical therapy* **86**, 726 (May, 2006).
4. R. D. Tucker-Seeley, S. V. Subramanian, Y. Li, G. Sorensen, Neighborhood safety, socioeconomic status, and physical activity in older adults. *Am J Prev Med* **37**, 207 (Sep, 2009).
5. P. Clarke, J. A. Ailshire, P. Lantz, Urban built environments and trajectories of mobility disability: findings from a national sample of community-dwelling American adults (1986-2001). *Soc Sci Med* **69**, 964 (Sep, 2009).
6. J. E. Gaugler, S. Duval, K. A. Anderson, R. L. Kane, Predicting nursing home admission in the U.S: a meta-analysis. *BMC geriatrics* **7**, 13 (2007).
7. M. Luppa *et al.*, Prediction of institutionalization in the elderly. A systematic review. *Age and ageing* **39**, 31 (Jan, 2010).

4. IMPACT

What was the impact on the development of the principal discipline(s) of the project?

We have expanded the knowledge of modifiable factors to preserve functional independence. Previously, little has been done to understand whether these factors are important among the cognitively impaired. We have comprehensively examined individual, family, as well as community-level factors that can be leveraged to optimize quality of life, prevent or delay dependencies, and minimize caregiver burden.

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

This project has identified several points of intervention that can be used to improve the health and well-being of those at risk for functional limitations and nursing home admissions. These findings are relevant for health care providers, patients, and family members of individuals with cognitive impairments or incipient dementia. Not smoking, being physically active, having spousal support, and residing in a safe, clean, cohesive neighborhood appear protective in preserving functional independence.

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

Nothing to Report

Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

6. PRODUCTS

- Published a manuscript on our results for cognitive impairment, individual-level modifiers and incident ADL limitations in *Neurology.*

  Rist PM, Capistrant BD, Wu Q, Marden JR, Glymour MM. Dementia and dependence: do modifiable risk factors delay disability? Neurology. 2014 Apr 29;82(17):1543-50. Epub 2014 Mar 28. Published. Acknowledgement of federal support (yes)

- Published a manuscript on our results for cognitive impairment, individual-level modifiers and incident IADL limitations in *Journal of Alzheimer's Disease.*

  Rist PM, Marden JR, Capistrant BD, Wu Q, Glymour MM, Do physical activity, smoking, drinking, or depression modify transitions from cognitive impairment to functional disability? J Alzheimers Dis. 2015;44(4):1171-80. Published, Acknowledgement of federal support (yes)

- Abstract entitled: "Forgetful but Not Disabled: Predictors of Incident IADL Limitations" was presented as a poster at the American Academy of Neurology Annual Meeting in Philadelphia April 26-May 3, 2014.

- Abstract entitled: "From forgetful to disabled: Does physical inactivity accelerate onset of IADL limitations among memory impaired adults?" was accepted for presentation as a poster an the upcoming Society for Epidemiologic Research Annual Meeting in Seattle June 24-27, 2014.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

NAME	Maria Glymour, ScD, MS
Project Role	Principal Investigator
Researcher Identifier	None
Nearest Person Month Worked	1.8
Contribution to Project	Principal Investigator
Funding Support	No other funding source provided funds for this project
Change in Active Support	Effective 3/1/15, Dr. Glymour began receiving 25% funding support on a Robert Wood Johnson Foundation award, "Launching the Culture of Health Investigator-Initiated Research program" Dr. Nancy E. Adler and David Vlahov, Project Directors. Dr. Glymour serves as an Associate Director and will provide a summary of the Culture of Health in Communities and participate, along with the directors, in the development of the PA and dissemination efforts.
Other Organizations Involved	Nothing to Report

NAME	Thu Thi Nguyen, PhD
Project Role	Specialist
Researcher Identifier	None
Nearest Person Month Worked	0.30
Contribution to Project	Dr. Nguyen has been lead analyst on this project, developing code to characterize neighborhood variables, integrating the 2006 and 2008 samples and validating the measures. She has implemented the models for neighborhood variables predicting onset of I/ADL limitations and begun drafting the manuscript for that work. She has also served as technical reviewer for the statistical code for the family level paper.
Funding Support	No other funding source provided funds for this project
Change in Active Support	Nothing to Report
Other Organizations Involved	Nothing to Report

NAME	Florencia Rojo
Project Role	Graduate Student

Researcher Identifier	None
Nearest Person Month Worked	0.18
Contribution to Project	Florencia Rojo has served as research assistant on the project, reviewing documentation on the variables, managing paperwork for the restricted data applications, and completing literature reviews, in addition to myriad smaller project related tasks.
Funding Support	No other funding source provided funds for this project
Change in Active Support	Nothing to Report
Other Organizations Involved	Nothing to Report

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

ACTIVE

(THIS AWARD)
UCSF/Glymour 04/20/13-04/19/16 1.80
Calendar
US ARMY W81XWH-12-1-0143
Social Resources that preserve functional independence after memory loss
Dr. Glymour uses a large, diverse, longitudinal study of middle aged and older Americans to identify modifiable social factors that help individuals preserve functional independence as long as possible, even in the context of declining memory or cognitive impairment.
Role: PI

UA-Birmingham/V. Howard 09/30/13 -05/31/16 1.20
Calendar
NIH/NIA 5RO1AG039588
Childhood SES Factors: Impact on age-related cognitive and vascular health
Dr. Glymour's primary roles are overseeing the data collection efforts for historical school quality measures,
working with the investigative team on collecting other measures of childhood adversity, and collaborating on
analyses and publications related to the project.
Role: PI of subcontract

Univ MN/T. Osypuk 09/12/13-09/11/15 1.20
Calendar
NIH/NIMHD 7RO1MD006064
Effect of a neighborhood experiment on youth behavior problems
Dr. Glymour assists with analytic issues related to variable creation, model building, and model interpretation related to the instrumental variable analysis of the experimental data.
Role: PI of subcontract

UCSF/N. Adler 03/01/15-02/28/18 3.00
Calendar
Robert Wood Johnson Foundation
Supporting a culture of health: The COHIR NPO
This grant establishes the National Program Office for the broad, innovative "culture of health investigator-initiated research" (COHIR) program of the RWJF at the Center for Health and Community at UCSF. We will put out a Call for Proposal and review grant applications and award grants to build the evidence to support a Culture of Health.
Role: Participating PI

PENDING

Brown/Jones 07/01/15-06/30/20 1.20
Calendar
NIH/ RFA-AG-15-015
Psychometric Integrative Technology for Cognitive Health Research
The goal of the project is to harmonize brief cognitive assessments across diverse international samples and advise on the optimal measures for harmonized cross-national cohorts sponsored.
Role: Co-Investigator

Univ WA/ Crane 07/01/15-6/30/17 0.72
calendar
NIH/NIA 1A01AG042437
Genetic architecture of memory and executive functioning in Alzheimer's disease
Dr. Glymour's primary role is to serve as an advisor on Mendelian Randomization studies.
Role: PI of subcontract

Univ WA/ Crane 09/01/16-8/31/19 0.60
Calendar
DOD
Lifecourse context, TBI and AD in veterans: combining the strengths of ACT and ADAPT
Dr. Glymour will work closely with Dr. Crane in specification of the proposed lifecourse and sensitive period analyses of the impacts of TBI on cognitive function and change and will work with the research team to implement analyses in the ACT cohort.
Role: PI of subcontract

Kaiser/Whitmer 12/01/15-11/30/20 1.20
calendar
Neuroepidemiology, causal inference in longitudinal observational data, health disparities, lifecourse epidemiology
Dr. Glymour will work closely with the PIs, Drs. Whitmer, Mungas, and Reed, in specification of the lifecourse models for cognitive decline, evaluating how time-varying exposures influence long-term trajectories.
Role: PI of subcontract

Univ MN/T. Osypuk 09/15/15-08/31/17 1.20
Calendar
NIH P0506737
Mediators and Moderators of a Neighborhood Experiment on Alcohol Use

Dr. Glymour will assist with implementing IV models using this RCT to evaluate neighborhood determinants of adolescent alcohol use.
Role: PI of subcontract

Overlap statement: In the event that all pending work is successfully funded, Dr. Glymour will reduce her effort on the UMN T. Osypuk project (NIH P0506737) and/or the UCSF/N. Adler project to ensure there is no overlap of effort.

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS: None

9. APPENDICES:

All figures and/or tables referenced in the body of the report under 3.

Table 1. Characteristics of Those Included in the Analysis of Dementia Probability Category and Any Incident ADL Limitation by Dementia Probability Category at first exposure wave.

Characteristic	High Dementia Probability (N=1032)	Low Dementia Probability (N=3093)
Age (mean, std)	76.1 (6.3)	71.5 (5.2)
Gender (% male)	56.4	39.1
Race (% black)	14.5	7.5
Southern birthplace (%)	15.8	12.3
Years of education (mean, std)	11.3 (3.2)	13.0 (2.6)
Mother had ≥8 years of education (%)	44.5	55.0
Father had ≥8 years of education (%)	39.9	47.1
Physically inactive (%)	54.8	48.5
Not drinking moderately (%)	78.8	71.2
Ever smoker (%)	59.2	56.1
Current depression (%)	10.3	7.4
Body mass index (mean, std)	25.8 (4.0)	26.2 (4.3)
Number of comorbidities (mean, std)	1.6 (1.2)	1.5 (1.1)
Living arrangement		
Live with spouse	55.0	62.7
Live with others/children	11.1	8.4
Live alone	33.9	28.9
Proximity to children		
Live with children	16.6	14.7
No children	7.6	7.5
Children within 10 miles	46.6	44.2
Children over 10 miles	29.3	33.6
Less than weekly contact with friends	37.7	39.1
Spouse's employment status		
Retired	34.80	39.5
Full time	2.1	4.2
Part time	6.5	10.3
Not working/disabled	11.6	8.7
No spouse	45.0	37.3
Spouse's depression status		
Not depressed	48.3	58.2
Depressed	6.8	4.5
No spouse	45.0	37.3
Spouse's educational status		
High school diploma/GED	36.1	37.2
College diploma or higher	6.8	14.9
Less than a high school diploma/GED	12.3	10.6
No spouse	44.9	37.3
Isolation Index		
Not isolated	38.4	39.8
Isolated (1 point)	45.5	46.2

Isolated (2 points)	15.5	12.8
Isolated (3 points)	0.9	1.2
Marital Status		
Not married	44.9	37.3
Married	55.1	62.7

Table 2. Association between family-level variables and risk of incident I/ADL limitations.

	ADL			IADL		
	OR	95%	CI	OR	95%	CI
Marital Status						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.63
Married	1.00	ref		1.00	ref	
Not married	1.14	1.01	1.30	1.04	0.92	1.18
Living Arrangement						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.63
Live with spouse	1.00	ref		1.00	ref	
Live with someone other than spouse	1.35	1.11	1.65	1.30	1.06	1.61
Live Alone	1.10	0.96	1.25	0.99	0.87	1.13
Proximity to Children						
Low dementia probability	0.76	0.66	0.88	0.56	0.49	0.64
Live with children	1.00	ref		1.00	ref	
No children	0.95	0.75	1.22	0.79	0.62	1.01
Children within 10 miles	0.89	0.75	1.05	0.93	0.79	1.11
Children over 10 miles	0.87	0.73	1.04	0.87	0.73	1.04
Contacts with friends						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.64
Weekly or more frequent contact	1.00	ref		1.00	Ref	
Less than weekly contact	1.03	0.92	1.15	1.06	0.95	1.19
Spouse's employment status						
Low dementia probability	0.76	0.66	0.87	0.56	0.48	0.64
Retired spouse	1.00	ref		1.00	ref	
Spouse employed full time	0.92	0.64	1.33	0.79	0.54	1.17
Spouse employed part time	0.98	0.79	1.22	0.93	0.75	1.17
Spouse not working	1.06	0.86	1.32	0.92	0.73	1.15
No spouse	1.14	1.001	1.31	1.01	0.89	1.16
Spouse's depression status						
Low dementia probability	0.77	0.67	0.88	0.56	0.48	0.64
Not depressed spouse	1.00	ref		1.00	ref	
Depressed spouse	1.56	1.21	2.00	1.23	0.93	1.63
No spouse	1.19	1.05	1.35	1.06	0.93	1.20
Spouse's educational status						
Low dementia probability	0.76	0.66	0.87	0.56	0.48	0.64
Spouse with less than high school education	1.29	1.06	1.57	0.83	0.68	1.01
Spouse with high school education	1.00	ref		1.00	Ref	
Spouse with college education	1.03	0.84	1.26	0.98	0.80	1.21
No spouse	1.23	1.06	1.43	0.99	0.86	1.14
Isolation Index						
Low dementia probability	0.76	0.66	0.87	0.55	0.48	0.64
Not isolated	1.00	ref		1.00	ref	
Isolated (1 point)	1.06	0.94	1.20	0.97	0.86	1.10
Isolated (2 points)	1.07	0.90	1.27	1.00	0.84	1.18
Isolated (3 points)	0.97	0.63	1.47	0.74	0.42	1.30

Table 3. Association between dementia probability and incident I/ADL limitations including interactions between dementia probability and individual health factors.

	ADL			IADL		
	OR	95%	CI	OR	95%	CI
Marital Status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.77	0.64	0.92	0.55	0.46	0.66
Not married	1.00	ref		1.00	ref	
Married	1.16	0.92	1.45	1.04	0.83	1.29
Married*low dementia probability	0.98	0.76	1.26	1.01	0.79	1.29
Living Arrangement						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.77	0.64	0.92	0.55	0.46	0.66
Live with spouse	1.00	ref		1.00	ref	
Live with someone other than spouse	1.22	0.83	1.78	1.24	0.86	1.77
Low dementia probability*Live with someone other than spouse	1.17	0.76	1.79	1.08	0.71	1.64
Live Alone	1.16	0.91	1.47	1.00	0.80	1.27
Low dementia probability*Live Alone	0.92	0.71	1.21	0.98	0.75	1.28
Proximity to Children						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.71	0.51	0.98	0.61	0.45	0.84
Live with children	1.00	ref		1.00	ref	
No children	0.70	0.45	1.11	0.72	0.47	1.10
Low dementia probability*No children	1.55	0.91	2.64	1.15	0.69	1.93
Children within 10 miles	0.89	0.65	1.21	1.00	0.74	1.33
Low dementia probability*Children within 10 miles	1.00	0.70	1.43	0.91	0.64	1.29
Children over 10 miles	0.80	0.57	1.12	1.00	0.73	1.38
Low dementia probability*Children over 10 miles	1.13	0.77	1.67	0.81	0.55	1.19
Contacts with friends						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.77	0.65	0.91	0.55	0.47	0.66
Weekly or more frequent contact	1.00	ref		1.00	ref	
Less than weekly contact	1.04	0.84	1.29	1.06	0.86	1.31
Low dementia probability*Less than weekly contact	0.98	0.76	1.26	1.00	0.78	1.28
Spouse's employment status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.83	0.67	1.04	0.54	0.44	0.67
Retired spouse	1.00	ref		1.00	ref	
Spouse employed full time	0.46	0.14	1.53	1.24	0.58	2.69
Low dementia probability*Spouse employed full time	2.15	0.61	7.55	0.57	0.23	1.38

Spouse employed part time	1.34	0.87	2.04	0.74	0.46	1.19
Low dementia probability*Spouse employed part time	0.67	0.41	1.10	1.35	0.79	2.30
Spouse not working	1.29	0.91	1.83	0.90	0.63	1.30
Low dementia probability*Spouse not working	0.74	0.48	1.15	1.02	0.65	1.59
No spouse	1.23	0.96	1.59	0.99	0.78	1.25
Low dementia probability*No spouse	0.90	0.68	1.20	1.04	0.79	1.36
Spouse's depression status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.76	0.63	0.92	0.54	0.45	0.65
Not depressed spouse	1.00	ref		1.00	ref	
Depressed spouse	1.42	0.92	2.18	1.11	0.69	1.79
Low dementia probability*Depressed spouse	1.16	0.68	1.97	1.18	0.66	2.11
No spouse	1.20	0.95	1.52	1.04	0.83	1.30
Low dementia probability*No spouse	0.99	0.76	1.28	1.03	0.80	1.32
Spouse's educational status						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.82	0.66	1.03	0.59	0.48	0.73
Spouse with less than high school education	1.49	1.05	2.11	0.93	0.66	1.31
Low dementia probability*Spouse with less than high school education	0.82	0.54	1.23	0.84	0.55	1.27
Spouse with high school education	1.00	ref		1.00	ref	
Spouse with college education	1.18	0.75	1.84	1.15	0.73	1.82
Low dementia probability*Spouse with college education	0.84	0.52	1.38	0.81	0.49	1.33
No spouse	1.32	1.02	1.71	1.02	0.80	1.31
Low dementia probability*No spouse	0.90	0.68	1.20	0.95	0.72	1.25
Isolation Index						
High dementia probability	1.00	ref		1.00	ref	
Low dementia probability	0.78	0.63	0.98	0.54	0.44	0.67
Isolation (1 pt)	1.13	0.90	1.43	0.96	0.76	1.20
Isolation (1 pt)*Low dementia probability	0.91	0.69	1.19	1.02	0.79	1.34
Isolation (2 pts)	1.01	0.73	1.40	0.93	0.69	1.27
Isolation (2 pts)*Low dementia probability	1.09	0.75	1.58	1.11	0.77	1.59
Isolation (3 pts)	1.02	0.56	1.85	0.83	0.28	2.44
Isolation (3 pts)*Low dementia probability	0.93	0.41	2.07	0.85	0.24	3.05

Table 4. Baseline characteristics of participants included in the analysis examining community-level factors and I/ADL limitations

Characteristic	ADL (n=9713)	IADL (n=9874)
Age (mean, std)	65.6 (9.8)	65.6 (9.9)
Gender (% male)	40.7	41.0
Race (% black)	12.1	11.7
Southern birthplace (%)	14.8	14.6
Years of education (mean, std)	13.2 (2.6)	13.2 (2.6)
Mother had ≥8 years of education (%)	62.5	62.89
Father had ≥8 years of education (%)	52.9	53.2
Marital Status, (%)		
Married	71.4	71.9
Divorced/separated	10.5	10.2
Widowed	15.4	15.1
Never married	2.7	2.7
Currently employed	45.3	45.7
Fair or poor self-rated health (%)	15.2	14.2
Physically inactive (%)	71.7	71.1
Alcohol consumption		
Non-drinker (%)	61.0	60.9
0-<2 drinks/day) (%)	32.4	32.6
>2 drinks/day)	6.6	6.5
Ever smoker (%)	56.1	56.0
Current depression (%)	0.1	0.1
overweight (BMI 25 - <30) (%)	40.0	40.6
obese (BMI > 30(%)	27.7	26.0
Memory function (score>1.3) (%)	31.89	32.17
Physical disorder (mean, std)	2.4 (1.3)	2.4 (1.3)
Cohesion (mean, std)	5.6 (1.3)	5.6 (1.3)
Social ties (mean, std)	0.5 (0.3)	0.5 (0.3)
Neighborhood safety (% excellent, very good, good)	93.2	93.47

Table 5. Association between neighborhood-level variables and incident ADL and IADL limitations

	ADL			IADL		
	OR	95% CI		OR	95% CI	
Physical disorder		(n=9072)			(n=9436)	
Memory	0.91	0.72	1.13	0.78	0.64	0.97
Disorder	1.06	1.01	1.12	1.10	1.04	1.16
Social cohesion		(n=9080)			(n=9446)	
Memory	0.90	0.72	1.13	0.78	0.63	0.96
Cohesion	0.96	0.91	1.01	0.91	0.86	0.95
Neighborhood safety		(n=9047)			(n=9412)	
Memory	0.89	0.71	1.11	0.78	0.63	0.96
Safety	0.88	0.69	1.11	0.68	0.52	0.88
Social ties		(n=8859)			(n=9220)	
Memory	0.88	0.70	1.11	0.73	0.59	0.91
Social ties	1.04	0.83	1.32	0.97	0.77	1.21

Table 6. Association between neighborhood-level variables and incident ADL and IADL limitations including interactions between neighborhood variables and memory function

	ADL			IADL		
	OR	95% CI		OR	95% CI	
Physical disorder		(n=9072)			(n=9436)	
Memory	0.83	0.56	1.23	0.79	0.53	1.18
Disorder	1.05	1.00	1.11	1.10	1.04	1.16
Memory*Disorder	1.04	0.90	1.19	1.00	0.86	1.16
Social cohesion		(n=9080)			(n=9446)	
Memory	0.58	0.24	1.40	1.00	0.45	2.23
Cohesion	0.94	0.90	0.99	0.92	0.87	0.97
Memory_d*Cohesion	1.08	0.93	1.26	0.96	0.83	1.09
Neighborhood safety		(n=9047)			(n=9412)	
Memory	0.64	0.31	1.30	1.05	0.53	2.09
Safety	0.82	0.64	1.05	0.72	0.55	0.94
Memory*Safety	1.42	0.69	2.91	0.72	0.36	1.45
Social ties		(n=8859)			(n=9220)	
Memory	0.74	0.50	1.11	0.74	0.50	1.10
Social Ties	0.96	0.75	1.22	0.97	0.76	1.23
Memory*Social Ties	1.38	0.76	2.51	0.98	0.53	1.82

Table 7. Odds ratios for prediction of nursing home admission as a function of dementia risk, physical inactivity, alcohol use, and ever smoking (N=7631)

	Nursing Home Admission		
	OR	95%	CI
Low Dementia Probability	0.29	0.24	0.36
Low Physical Activity	1.52	1.35	1.71
No Alcohol Consumption	1.36	1.17	1.57
Ever Smoking	0.99	0.88	1.11

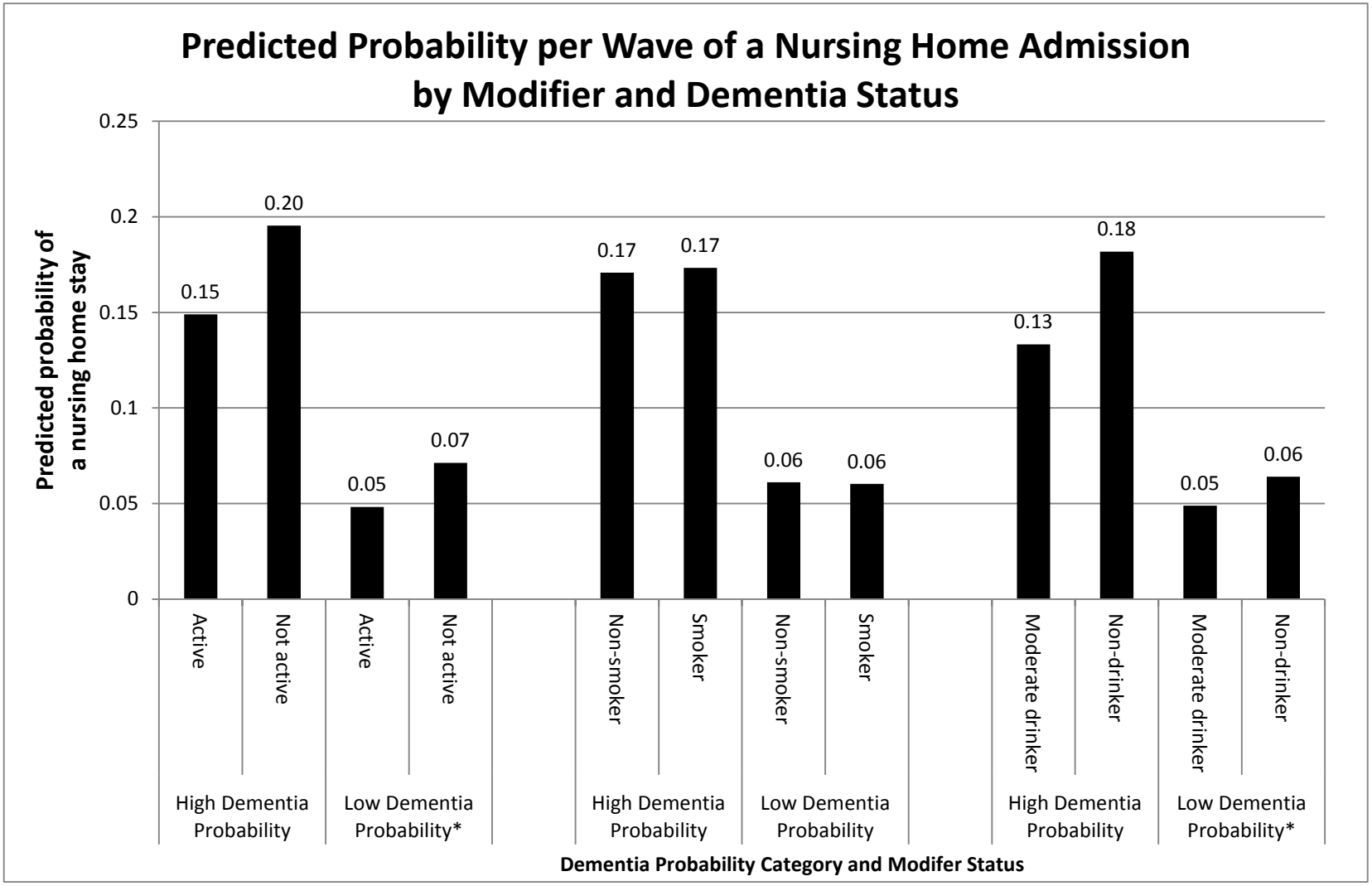
Note: Model is simultaneously adjusted for all of the risk factors.

Table 8. Association between dementia probability category and nursing home admission including interactions between dementia probability and each risk factor (N=7,631)

	Nursing Home Admission		
	OR	95%	CI
Physical Activity			
Low Dementia Probability	0.28	0.19	0.40
Low Dementia Probability*Low Physical Activity	1.08	0.71	1.66
Low Physical Activity	1.41	0.94	2.13
Alcohol Consumption			
Low Dementia Probability	0.32	0.17	0.58
Low Dementia Probability*No Alcohol Consumption	0.90	0.48	1.69
No Alcohol Consumption	1.50	0.81	2.78
Smoking			
Low Dementia Probability	0.30	0.23	0.39
Low Dementia Probability*Ever Smoking	0.97	0.68	1.38
Ever Smoking	1.02	0.73	1.43

Note: Models all include all of the other risk factors, but do not include interaction terms between the other risk factors and dementia probability. Interaction terms test the null that the relative effect of the risk factor is the same for individuals with high and low dementia probability.

Figure 1. Predicted probability of nursing home admission per wave, by modifier and dementia probability category.



* Indicates a statistically significant difference between those with and without the modified